## HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 1 of 8 Title METHODS FOR THE PRODUCTION OF REDOX

PROTEINS.
Applicant van Rooijen et al.
Serial No. 10/032,201 Filed: December 19, 2001
Our Docket No: 38814-351B

10	20 30 4	
	CACAACACAAGGCTCTCTATC	O 50 60 GTAGGAAGTGGCCCAGCGGCA
70	80 90 10	
	GCAGCTAGGGCTGAACTTAAA	CCTCTTCTCTCTTCCAACCAACCA
130	140 150 16	
TR A T G G C T A A C G A C A T C G C T ATTHIREDB A T G G C T A A C G A C A T C G C T	CCCGGTGGTCAACTAACTAACCAACC	
190	200 210 22	
TR CCCGGATTTCCAGAAGGT ATTHIREDB CCCGGATTTCCAGAAGGT	ATTCTCGGAGTAGAGCTCACT	C
250	260 270 28	0 390 300
	ATATTACAGAGACGGTGACG	AAAGTCGATTTCTCTTCAAAA
310	320 330 34	
TR CCGTTTAAGCTATTCACA ATTHIREDB CCGTTTAAGCTATTCACA	GATTCAAAAGCCATTCTCCCT	CACCCMCMCAMMCMCCCCMAICM
	380 390 40	
TR GGAGCTGTGGCTAAGCGGATTHIREDBGGAGCTGTGGCTAAGTGG	CTTAGCTTCGTTGGATCTCCT	
	440 450 46	
TR A A C C G T G G A A T C T C C G C T ATTHIREDB A A C C G T G G A A T C T C C G C T	TGTGCTGTTTGCGACGCACCT	CCTCCCATATTCCCCTTAACAAA
	500 510 52	
TR CCTCTTGCGGTGATCGGTATTHIREDBCCTCTTGCGGTGATCGGT	GGAGGCGATTCACCAATCCAA	
550	560 570 58	0 590 600
TR TATGGATCTAAAGTGTAT ATTHIREDS TATGGATCTAAAGTGTAT	ATAATCCATAGGAGAGATGCT	TTTAGAGCCCTCTAACATTATC
	620 630 64	
TR CAGCAGCGAGCTTTGTCT ATTHIREDB CAGCAGCGAGCTTTGTCT	AATCCTAAGATTGATGTGATT	TCCAACTCCTCTCTTCTTCTX
	680 690 70	
TR GCTTATGGAGATGGAGAA ATTHIREDB GCTTATGGAGAT	AGAGATGTGCTTGGAGGATTG	A A A C T C A A C A A T C T C C T T A A C C
730	740 750 76	270
TR GGAGATGTTTCTGATTTA ATTHIREDB GGAGATGTTTCTGATTTA	AAAGTTTCTGGATTGTTCTT	CCTATTCCTCATCACCT
	800 810 82	
ATTHIREDB A C C A A G T T T T T G G A T G G T	GGTGTTGAGTTAGATTACATT	
	860 870 88	
	G T T C C C G G A G T T T T C C C T C C C	
910	920 930 94	050
TR TATAGGCAAGCCATCACT	GCTGCAGGAACTGGGTGCATC	
970	980 990 1000	1010
TR TACTTACAAGAGATTGGA	TCTCAGCAAGGTAAGAGTCAT	P.C.A.
The state of the s	- C - C - C - A - G - G - G - G - G - G - G - G - G	I G A

FIG. I

HELLER EHRMAN WHITE & MCAULIFFE LLP
Sheet 2 of 8

Title METHODS FOR THE PRODUCTION OF REDOX
PROTEINS.

Applicant van Rooijen et al.
Serial No. 10/032,201 Filed: December 19, 2001
Our Docket No.: 38814-351B

ALTHIKEDBENG LETHNTRLCIVGSGPAAHTAAIYAARBELKPLLFEGWM	ANDIAPGGQLTITDVENE
Of ATTHIREDB PGFPEGILGVELTDKFRKQSERFGTTIFTETVTKVDFSSKP Of TR	110 FKLFTDSKAILADAVILA FKLFTDSKAILADAVILA
ATTHIREDB G A V A K W L S F V G S G E V L G G L W N R G I S A C A V C D G A A P I F R N K P TR	LAVIGGGDSAMEEANFLTK LAVIGGGDSAMEEANFLTK
GSKVYII DRRDAFRASKIMQQRALSNPKIDVIWNSSVYEA GSKVYII HRRDAFRASKIMQQRALSNPKIDVIWNSSVYEA	Y G D G E R D V L G G L K V K N V V T Y G D G E R D V L G G L K V K N V V T
250 270 250 260 ATTHIREDB G D V S D L K V S G L F F A I G H E P A T K F L D G G V E L D S D G Y V V T K P G O T T R T L D G G V E L D S D G Y V V T K P G O T T R T L D G G V E L D S D G Y V V T K P G O T T R T L D G G V E L D S D G Y V V T K P G O T T R T R T L D G G V E L D S D G Y V V T K P G O T T R T L D G G V E L D S D G Y V V T K P G O T T R T R T L D G G V E L D S D G Y V V T K P G O T T R T R T L D G G V E L D S D G Y V V T K P G O T T R T R T L D G G V E L D S D G Y V V T K P G O T T R T R T R T L D G G V E L D S D G Y V T K P G O T T R T R T R T R T R T R T R T R T R	T T Q T S V P G V F A A G D V Q D K K T T Q T S V P G V F A A G D V Q D K K
310 YRQAITAAGTGCMAALDAEHYLQEIGSQQGKSD YRQAITAAGTGCMAALDAEHYLQEIGSQQGKSD	350

PROTEINS.

Applicant van Rooijen et al. Serial No. 10/032,201 Filed: December 19, 2001

Our Docket No.: 38814-351B

HELLER EHRMAN WHITE & MCAULIFFE LLP

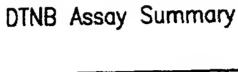
Sheet 4 of 8

Title METHODS FOR THE PRODUCTION OF REDOX PROTEINS.

Applicant van Rooijen et al.

Serial No. 10/032,201 Filed: December 19, 2001

Our Docket No.: 38814-351B



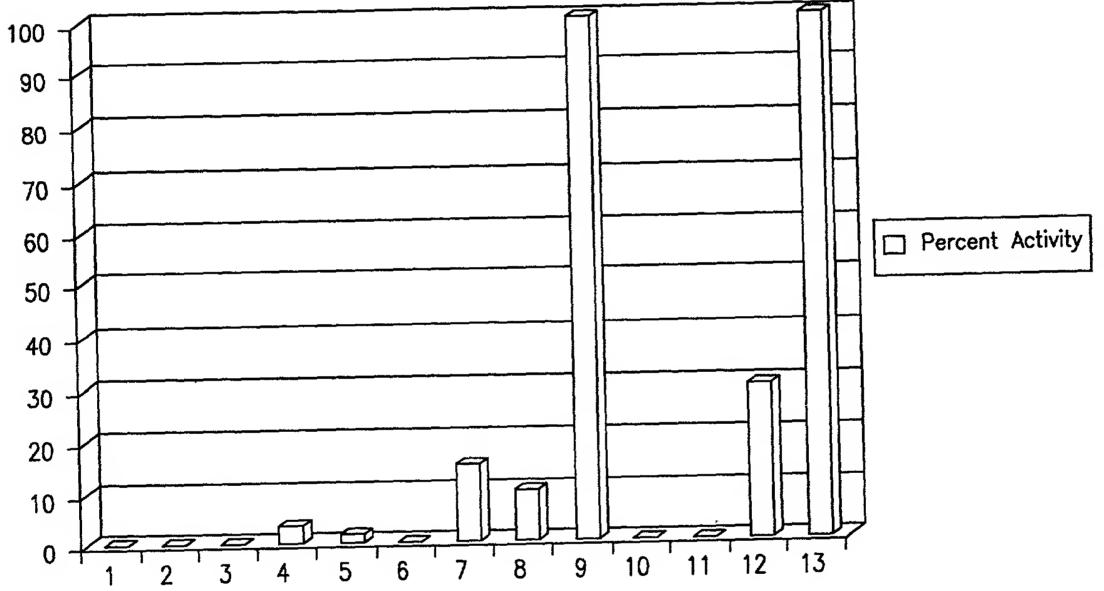


FIG. 4

### HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 5 of 8 Title METHODS FOR THE PRODUCTION OF REDOX

PROTEINS.

Applicant van Rooijen et al. Serial No. 10/032,201 Filed: December 19, 2001 Our Docket No.: 38814-351B

#### **HETEROMULTIMERS**

Class	Heteromultimer	Example sequence reference for
		heteromultimeric subunits
Biosynthetic	3-methyl-2-oxobutanoate	McKean, et al. Biochim. Biophys. Acta (1992)
	dehydrogenase (2-oxoisovalerate	1171:109-112 / Chuang, J.L., et al FEBS Lett. a
	dehydrogenase (lipoamide))- E1 component)	(1990) 262 (2), 305-309.
Biosynthetic	3-oxoadipate CoA-transferase	Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992)
Biosynthetic	anthronilate synthogogindolo 2 alumani	174:4657-4666
	anthranilate synthase:indole-3-glycerol phosphate synthase	Zalkin, H.; et al. J. Biol. Chem. (1984) 259:3985-3992.
Biosynthetic	beta-ketoacyl-[acyl carrier protein] synthase I	Siggaard-Andersen, M. et al. Proc. Natl. Acad. Sci. U.S.A. (1991) 88:4114-4118
Biosynthetic	butyrateacetoacetate CoA-transferase	Fischer, R.J., et al. J. Bacteriol. (1993) 175 (21), 6959-6969.
Biosynthetic	cAMP dependent protein kinase	Mutzel, R et al. Proc. Natl. Acad. Sci. U.S.A. (1987)
		84:6-10./ Burki, E., et al. Gene (1991) 102 (1), 57-
		65.
Biosynthetic	carbamoyl-phosphate synthase	Shigenobu, S., et al. Nature. (2000) 407 (6800), 81-86.
Biosynthetic	Creatine kinase	Billadello, J.J.; et al. Biochem. Biophys. Res.
		Commun. (1986) 138:392-398. / Roman, D.; et al.
		Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.
Biosynthetic	gamma-glutamyltransferase (gamma-	Papandrikopoulou, A.; et al. Eur. J. Biochem.
	glutamyl transpeptidase)	(1989) 183:693-698.
Biosynthetic	glutathione transferase	Morrow, C.S. et al. Gene (1989) 75:3-11
Biosynthetic	glycerol-3-phosphate dehydrogenase	Cole, S.T. et al. J. Bacteriol. (1988) 170:2448-2456.
Biosynthetic	guanylate cyclase	Hinsch, K.D. et al. FEBS Lett. (1988) 239:29-34/ Koesling, D. et al. FEBS Lett. (1990) 266:128-132.
Biosynthetic	heterodisulfide reductase	Smith, D.R., et al. J. Bacteriol. (1997) 179 (22), 7135-7155.
Biosynthetic	human cathepsin	
Biosynthetic	Hydrogenase	Ritonja, A. et al. FEBS Lett. (1988) 228:341-345.
		Menon, N.K. et al. J. Bacteriol. (1990) 172:1969- 1977.
Biosynthetic	Meprin A	Johnson, G.D. and Hersh, L.B. J. Biol. Chem. (1992) 267:13505-13512.
Biosynthetic	methionine adenosyltransferase	Horikawa, S.; Tsukada, K. FEBS Lett. (1992) 312:37-41.
Biosynthetic	methylmalonyl-CoA mutase	Jackson, C.A. et al. Gene (1995) 167:127-132.
Biosynthetic	mitochondrial processing peptidase	Pollock, R.A. et al. EMBO J. (1988) 7:3493-3500.
Biosynthetic	Na+/K+-exchanging ATPase	Shull, G.E., et al. Biochemistry (1986) 25 (25),
		8125-8132./Mercer,R.W., et al.
		Mol. Cell. Biol. (1986) 6 (11), 3884-3890./
		Mercer, R.W., et al. J. Cell Biol. (1993) 121 (3),
		579-586.
Biosynthetic	NAD(+)-dependent isocitrate	Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem.
	dehydrogenase	(1992) 267:16417-16423. /Cupp, J.R. and
		McAlister-Henn, L.
		J. Biol. Chem. (1991) 266:22199-22205.
Biosynthetic	phosphoribosylformylglycinamidine	Ebbole, D.J.; Zalkin, H. J. Biol. Chem. (1987)
	synthase	262:8274-8287.
Biosynthetic	protocatechuate 3,4-dioxygenase	Frazee, R.W.; et al. J. Bacteriol. (1993) 175:6194-
	. and the state of	6202.

FIG. 5A

#### HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 6 of 8

Title METHODS FOR THE PRODUCTION OF REDOX PROTEINS.

Applicant van Rooijen et al.

Serial No. 10/032,201 Filed: December 19, 2001

Our Docket No.: 38814-351B

		31:10258-10264. / Allore, R.J.; et al. J. Biol. Chem. (1990) 265:15537-15543.
Biosynthetic	sucrosefructan 6-fructosyltransferase	Sprenger, N.; et al. Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.
Biosynthetic	Superoxide dismutase	Capo, C.R.; et al. Biochem. Biophys. Res. Commun. (1990) 173:1186-1193.
Biosynthetic	Urease	Labigne, A.; et al. J. Bacteriol. (1991) 173:1920-1931.
Biosynthetic	urokinase-type plasminogen activator (urokinase)	Belin, D. et al. Eur. J. Biochem. (1985) 148:225-232.
Biosythetic	methylmalonyl-coenzyme A mutase	Birch, A., et al J. Bacteriol. (1993) 175 (11), 3511-3519.
Calcium binding	Calcineurin	Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. et al. DNA (1989) 8:675-682.
Calcium binding	Calgranulin	Imamichi, T. et al. Biochem. Biophys. Res. Commun. (1993) 194:819-825.
Calcium binding	Calpain	Aoki, K. et al. FEBS Lett. (1986) 205:313-317.
DNA binding	AP1	van Straaten, F., et al. Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. /Hattori, K., et al Proceedings of the National Academy of Sciences of the United States of America. (1988) 85 (23), 9148-9152.
DNA binding	сМус-Мах	Schreiber-Agus, N et al. Mol. Cell. Biol. (1993) 13 (5), 2765-2775.
DNA binding	DNA binding protein HU-1/HU-2	Laine, B. et al. Eur. J. Biochem. (1980) 103:447-461.
DNA binding	hepatic nuclear factor 1	Bach, I. et al. Nucleic Acids Res. (1992) 20 (16), 4199-4204. / Rey-Campos, J. et al. EMBO J. (1991) 10 (6), 1445-1457.
DNA binding	Integration host factor	Miller, H.I. Cold Spring Harbor symposia on quantitative biology. (1984) 49, 691-698. / Flamm, E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117-128.
DNA binding	Ku	Reeves, W.H. and Sthoeger, Z.M. J. Biol. Chem. (1989) 264 (9), 5047-5052.
DNA binding	MutS	J. Biol. Chem. (1989) 264 (23), 13407-13411.  Bocker et al. 1999. Cancer Research 59, 816-822.
DNA binding	NF-E2	Chan, J. Y. et al Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370./ Toki, T., et al. Oncogene (1997) 14 (16), 1901-1910.
DNA binding	nuclear factor kB (NFkB)	Kieran M, et al. Cell. (1990) Sep 7;62(5):1007-18. / Ruben SM, et al. Science (1991) Mar 22;251(5000):1490-3. Erratum in: Science (1991) Oct 4;254(5028):11
Electron transport	corrinoid/iron-sulfur protein	Lu, W.P. et al. J. Biol. Chem. (1993) 268:5605- 5614.
Electron transport	cytochrome d ubiquinol oxidase	Green, G.N. et al. J. Biol. Chem. (1988) 263:13138-13143.
Electron transport	cytochrome-c3 hydrogenase	Menon, N.K. et al. J. Bacteriol. (1987) 169:5401-5407.
Electron transport	electron transfer flavoprotein	Finocchiaro, G. et al. Biol. Chem. (1988) 263:15773-15780. / Finocchiaro, G. et al. Eur. J. Biochem. (1993) 213:1003-1008.

FIG. 5B

# HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 7 of 8 Title METHODS FOR THE PRODUCTION OF REDOX PROTEINS.

Applicant van Rooijen et al. Serial No. 10/032,201 Filed: December 19, 2001

	-,		100011
Our Docket No.	: 388	14-3511	3

Electron transport	xylene monooxygenase	Shaw, J.P. and Harayama, S. Eur. J. Biochem.
•		(1992) 209:51-61. / Kasai, Y., et al. J. Bacteriol.
		(2001) 183 (22), 6662-6666.
Growth factor	hepatocyte growth factor	Nakamura, T. et al. Nature (1989) 342:440-443.
Growth factor	human chorionic gonadotropin	Morgan, F.J. et al. J. Biol. Chem. (1975) 250 (13), 5247-5258.
Growth factor	Platelet-derived growth factor	Takimoto, Y., et al. Hiroshima J. Med. Sci. (1993) 42 (1), 47-52./ Josephs, S.F., et al. Science (1984) 225 (4662), 636-639.
Hormone	Bombyxin	Adachi, T. et al. J. Biol. Chem. (1989) 264:7681-7685.
Hormone	Follicle stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Watkins, P.C., et al. DNA (1987) 6 (3), 205-212.
Hormone	Insulin	Bell,G.I., Pictet,R.L., Rutter,W.J., Cordell,B., Tischer,E. and Goodman,H.M. Sequence of the human insulin gene. Nature. 284 (5751), 26-32 (1980)
Hormone	Luteinizing Hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Shome, B. and Parlow, A.F. J. Clin. Endocrinol. Metab. (1973) 36 (3), 618-621.
Hormone	Thyroid stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, et al. FEBS Lett. (1985) 188 (2), 394-400.
Immune	B-cell antigen receptor complex	Hashimoto, S. et al. J. Immunol. (1993) 150 (2), 491-498. / Flaswinkel, H. and Reth, M. Immunogenetics (1992) 36 (4), 266-269.
Immune	Cell surface CD8 molecules	Ureta-Vidal, A., et al. Immunogenetics (1999) 49 (7-8), 718-721.
Immune	human complement subcomponent C1q	Sellar, G.C. et al. Biochem. J. (1991) 274:481-490.
Immune	T cell receptor	Talken, B.L. et al. Scand. J. Immunol. (2001) 54 (1-2), 204-210.
Photosynthesis	C-phycocyanin	Offner, G.D. et al. J. Biol. Chem. (1981) 256:12167-12175. / Troxler, R.F. et al. J. Biol. Chem. (1981) 256:12176-12184.
Photosynthesis	ferroredoxin-thioredoxin reductase	Chow, L.P. et al. Eur. J. Biochem. (1995) 231:149- 156. / Iwadate, H. et al. Eur. J. Biochem. (1994) 223:465-471.
Photosynthesis	Light harvesting complex I	Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.
Photosynthetic	cytochrome b559	Carrillo, N. et al. Curr Genet. 1986;10(8):619-24.
Protease	ATP-dependent Clp protease	Gerth, U. et al. Gene (1996) 181:77-83. / Kunst,F. et al. Nature (1997) 390 (6657), 249-256.
Receptor	alpha-2-macroglobulin receptor	Strickland, D.K. et al. J. Biol. Chem. (1990) 265:17401-17404. / Strickland, D.K. et al. J. Biol. Chem. (1991) 266:13364-13369.
Receptor	Interleukin-2 receptor	Ishida, N. et al. Nucleic Acids Res. (1985) 13:7579-7589. / Hatakeyama, M. et al. Science (1989) 244:551-556 / Takeshita, T. et al. Science (1992) 257:379-382.
Receptor	platelet-derived growth factor receptor	Lee, K.H. et al. Mol. Cell. Biol. (1990) 10:2237-2246. / Herren, B. et al. Biochim. Biophys. Acta 1173 (3), 294-302 (1993).
Structural	Hemoglobin	Heindell, H.C. et al. Cell (1978) 15 (1), 43-54.

HELLER EHRMAN WHITE & MCAULIFFE LLP
Sheet 8 of 8
Title METHODS FOR THE PRODUCTION OF REDOX

PROTEINS.

Applicant van Rooijen et al. Serial No. 10/032,201 Filed: December 19, 2001 Our Docket No.: 38814-351B

		Best, J.S. et al. Hoppe-Seyler's Z. Physiol. Chem. (1989) 350 (5), 563-580. / Hardison, R.C. J. Biol.
		Chem. (1981) 256 (22), 11780-11786.
Structural	human platelet glycoprotein Ib	Wenger, R.H. et al. Biochem. Biophys. Res.
		Commun. (1988) 156 (1), 389-395. / Yagi, M. et al.
		J. Biol. Chem. (1994) 269 (26), 17424-17427.
Structural	Plasma fibronectin	Kornblihtt, A.R. et al. Proc. Natl. Acad. Sci. U.S.A.
		(1983) 80:3218-3222.
Structural	Spectrin	Sahr, K.E. et al. J. Biol. Chem. (1990) 265:4434-
		4443. / Winkelmann, J.C. et al. J. Biol. Chem.
		(1990) 265:11827-11832.
Structural	Tubulin	Ponstingl, H. et al. Proc. Natl. Acad. Sci. U.S.A.
		(1981) 78:2757-2761. / Krauhs, E. et al. Proc. Natl.
		Acad. Sci. U.S.A. (1981) 78:4156-4160.
Toxin	Agkisacutacin	Cheng, X. et al. Biochem. Biophys. Res. Commun.
		(1999) 265 (2), 530-535.
Toxin	Beta bungarotoxins	Kondo, K. et al. J. Biochem. (1978) 83:101-115.
Toxin	Crotoxin	Bouchier, C. et al. Nucleic Acids Res. (1988) 16
		(18), 9050.
Toxin	Mojave toxin	John, T.R. et al. Gene (1994) 139:229-234.
Toxin	venom protein C9S3	Rowan, E.G. et al. Nucleic Acids Res. (1990)
		18:1639. / Joubert, F.J. and Viljoen, C.C. Hoppe-
		Seyler's Z. Physiol. Chem. (1979) 360:1075-1090.
Miscellaneous	Inhibin	Forage, R.G. et al. Proc. Natl. Acad. Sci. U.S.A.
		(1986) 83:3091-3095.
Miscellaneous	Monellin	Frank, G. and Zuber, H. Hoppe-Seyler's Z. Physiol.
		Chem. (1976) 357:585-592.
Miscellaneous	mRNA capping enzyme	Niles, E.G. et al., J. Virology (1986) 153:96-112.
Miscellaneous	Soybean insulin-binding protein si30	Barbashov, S.F. et al. Bioorg. Khim. (1991) 17:421-
		423.

FIG. 5D